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NEUROPHARMACOLOGICAL EVALUATION OF TOXIC CHEMICALS

PART I BEHAVIORAL AND EEG CORRELATES OF IMMOBILIZATION IN THE RHESUS MONKEY

PART II OPERANT CONDITIONING OF 12-15 Hz SENSORIMOTOR CORTEX EEG ACTIVITY IN THE RHESUS MONKEY

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FOR THE COMMANDER

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Two separate studies were carried out with two groups of four adult Rhesus monkeys. In the first, specific behaviors were quantified and compared in these animals under three conditions: (1) individually caged, (2) placed in primate restraint chairs, and (3) further immobilized with arm restraints. Behavior was generally attenuated in a progressive manner with increasing restraint. The chaired and arm restrained animal displayed an "immobilization response" characterized by cessation of movement, reduction of tone in all

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limbs and eye closure. This response was correlated specifically with a significant increase in rhythmic 12-15 Hz EEG activity over sensorimotor cortex, as determined by quantified power-spectral estimates. Evidence provided suggests an interaction between brain substrates of immobility and attention-relaxation.

In the second study, four monkeys were prepared surgically for central cortical EEG operant conditioning, as described previously in cats. Food reward was provided for criterion trains of sensorimotor cortex 12-15 Hz activity. All animals demonstrated acquistion of this EEG response. The behavior associated with this learning involved reduction of movement and muscle tone, similar to that observed in the immobilization response described above. Thus, feedback training of EEG patterns associated with immobility can be used to produce this response, and its central nervous system substrates in a systematic manner. This model will be utilized to further explore the central mechanism of monomethylhydrazine induced seizures and the protective effects of central cortical EEG feedback training demonstrated previously in cat and man.

PREFACE

This research was initiated by the Toxicology Branch, Toxic Hazards Division, Aerospace Medical Research Laboratory, under Project 7163. Experiments were performed under Contract AF F33615-76-C-5014, 8/1/75 to 7/31/78, by the School of Medicine, University of California, Los Angeles, California 90024.

The experiments were conducted by M. B. Sterman, Ph.D., of the Veterans Administration Hospital, Sepulveda, California 91343, S. J. Goodman, M.D. of Harbor General Hospital, Torrance, California 90509, and M.D. Fairchild, Ph.D., of the Veterans Administration Hospital, Long Beach, California 90804. Kenneth C. Back, Ph.D., was contract monitor for the Aerospace Medical Research Laboratory.

PART 1. BEHAVIORAL AND ELECTROENCEPHALOGRAPHIC CORRELATES OF IMMOBILIZATION IN THE RHESUS MONKEY

INTRODUCTION

The rhesus monkey (Macaca mulatta) has been utilized as an experimental subject in behavioral and biological research more often than any other species of subhuman primate. The development of the primate restraint chair provided an important technical advance in this regard, especially when procedures involving catheterization of the cardiovascular system or electrical stimulation or recording of brain were desired in awake, unsedated animals. The restraint chair minimizes the number of handling/capturing episodes and permits convenient and safe access to the animal while limiting the animal's access to implanted devices.

Though the restraint chair has become a standard tool in primate research, there are numerous major psychobiological alterations imposed upon the monkey by severe restriction in activity attendant upon its use. Since most primate societies are very mobile and are based on high-order social organization, housing in individual cages is an obvious contrast to their natural environment. Further, confinement in a primate chair not only drastically reduces freedom of movement, but also prevents intraspecific interaction and self-protecting survival behavior. Despite these obvious alterations in activity and behavioral repertoire, there have been few attempts at systematic study of the effects of such restraint.

During the course of several experiments, we were impressed with the occurrence of moderate behavioral changes when the monkeys were confined to chairs and of striking behavioral changes when the chaired monkeys were further restricted by arm restraint. Since we had observed a similar behavioral stillness in cats and man as a correlate of learned production of 12-15 Hz activity over the sensorimotor cortex (the sensorimotor rhythm, or SMR), we postulated that such SMR activity might appear as a spontaneous response to imposed immobilization (Wyrwicka and Sterman, 1968; Sterman et al., 1969; Sterman et al., 1974). Furthermore, it has been established that immobilization, restraint and operantly trained enhancement of the SMR in cats all resulted in a significant elevation of convulsive thresholds associated with exposure to monomethylhydrazine (Sterman et al., 1972; Sterman, 1976; Bowersox et al., in press). Accordingly, it was deemed important to determine the relationship between behavioral and EEG responses to restraint in the rhesus monkey prior to exploring the influence of MMH upon these parameters.

METHODS

BEHAVIORAL STUDY

In Condition 1, semi-free-ranging monkeys maintained in individual cages were observed, and behavior was categorically described according to criteria developed during a preliminary phase of the study (Table 1). In Condition 2 the animals were observed during chair restraint, and in

Condition 3 further immobilization occurred by restraining the arms to the side of the chair using leather bracelets (Figure 1). The same behavioral categories were scored for each animal in all 3 conditions.

TABLE 1

Behavioral categories analyzed under varying conditions of restraint.

EYES	Blink	EB	Eyelids slowly close over eyes but remain closed only briefly.
	Closed	EC	Eyelids close over eyes and remain closed.
	Observer	EO	Eye contact with observer.
	Focus	EF	Eyes focus on environment (as opposed to listless gazing).
MOUTH	Closed	MC	Mouth closed in a relaxed manner.
	Open	MO	Mouth open in mild threat gesture, sometimes with teeth bared.
	Lipsmack	ML	Lips pursed forward and rapidly making chewing movements.
	Vocalization	MV	Any noise emitted other than cough or sneeze.
HEAD	Still	HS	Head remains in one position.
	Movement	HM	Head bobs or turns in rapid change of position.
LIMBS	Manipulation	LM	Use hands or feet to handle an object.
	Reposition	LR	Use limbs to alter body position.
	Still	LS	Limbs remain relaxed and unused.

EEG STUDY

Three monkeys were prepared with cortical electrodes implanted over the sensorimotor cortex. EEG data were then collected while the animals sat quietly in the primate chair (Baseline), while the animals were aroused by noise (Alert), while the animals' arms were restrained (Immobilization), while the animals were arm restrained and aroused (Immobilization + Alert), and finally while the animals again sat quietly (Baseline). EEG recordings were collected simultaneously on an ink-writer polygraph and on magnetic tape. All recordings were bipolar, in a rostrocaudal array, spanning the central sulcus between electrodes equidistant from midline. The signal from the tape was later electronically prefiltered between 015 and 40 Hz and digitized at a rate of 102.4 samples per second. A Fast Fourier Transform was then used to calculate power spectral estimates for each 17.5-second epoch of data. A three-point moving average filter was applied to the resulting spectra, and each spectrum was plotted isometrically (Bickford et al., 1972).

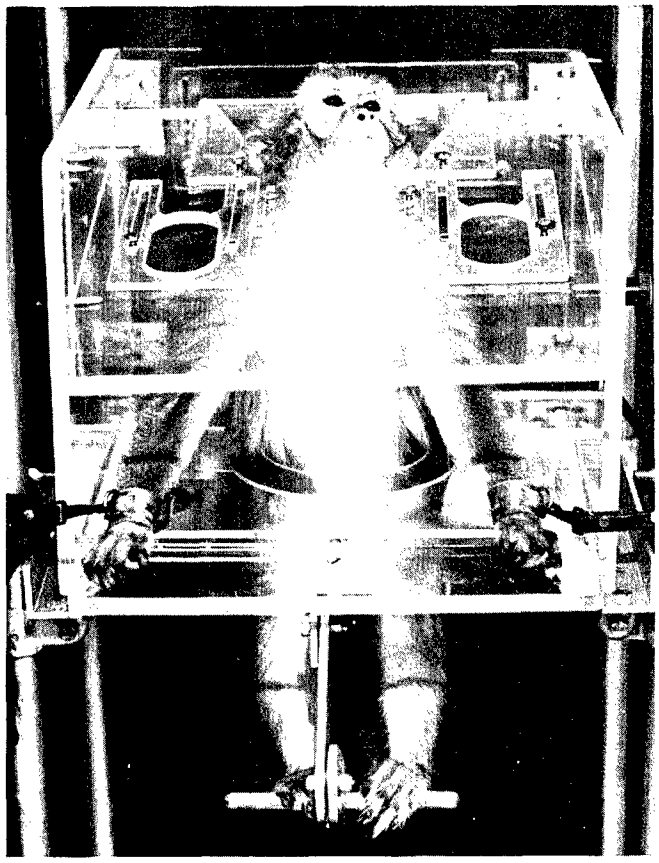

Figure 1. Immobilization of monkey. Animal is in a standard primate chair. The waist plate is in a "yoked" position so that the legs cannot be flexed against the abdomen. Snugly applied leather bracelets have been used to extend the arms into a relatively immobilized position.

RESULTS

BEHAVIORAL STUDY

Behavior characteristic of the caged animal was markedly decreased in the primate chair, as summarized quantitatively in Table 2 and graphically in Figure 2. Binding the wrists resulted in an even more dramatic change with further reduction of activities characteristic of a caged animal accompanied by the appearance of behavior infrequently observed in caged animals. The animals could best be characterized as atypically inactive with closed eyes (Figure 3).

TABLE 2

Behavioral changes under varying conditions of restraint.

Part 1: Frequency of Behaviors

	Behavior		Condition 1 Mean (SEM)+	Condition 2 Mean (SEM)+	Condition 3 Mean (SEM)+
EYES	Blink	EB	0.8 (0.4)	10.3 (2.6)	22.3 (4.6)
	Closed	EC	0.0 (0.0)	3.5 (0.9)	6.2 (2.9)
	Observer	EO	11.9 (5.0)	3.7 (2.6)	0.8 (0.8)
	Focus	EF	39.8 (14.6)	7.3 (2.4)	3.5 (2.6)
MOUTH	Closed	MC	8.8 (4.0)	20.0 (3.1)	25.0 (0.0)
	Open	MO	8.8 (5.0)	3.6 (2.9)	0.5 (0.2)
	Lipsmack	ML	9.7 (4.4)	7.8 (4.1)	0.7 (0.7)
	Vocalization	MV	2.3 (1.0)	0.2 (0.6)	0.0 (0.0)
HEAD	Still	HS	0.0 (0.0)	12.5 (5.6)	16.7 (8.4)
	Movement	HM	13.9 (4.8)	2.9 (1.6)	0.3 (0.3)
LIMBS	Manipulation	LM	11.9 (2.6)	1.4 (1.4)	0.0 (0.0)
	Reposition	LR	13.8 (5.7)	4.2 (1.7)	0.5 (0.5)
	Still	LS	6.5 (1.5)	15.0 (2.6)	25.0 (0.0)

Part 2: Eyelid Closure Behavior

Behavior	Condition 1 Mean (SEM)+	Condition 2 Mean (SEM)+	Condition 3 Mean (SEM)+
EC Frequency/Session	0.0 (0.0)	6.3 (3.5)	21.3 (3.8)
EC Epoch Duration, sec.	0.0 (0.0)	3.9 (2.3)	9.7 (1.9)
Latency to EC, min.	15.0 (15.0)	9.8 (3.3)	2.5 (1.0)
Total duration EC, %	0.0 (0.0)	5.3 (3.1)	22.3 (4.7)

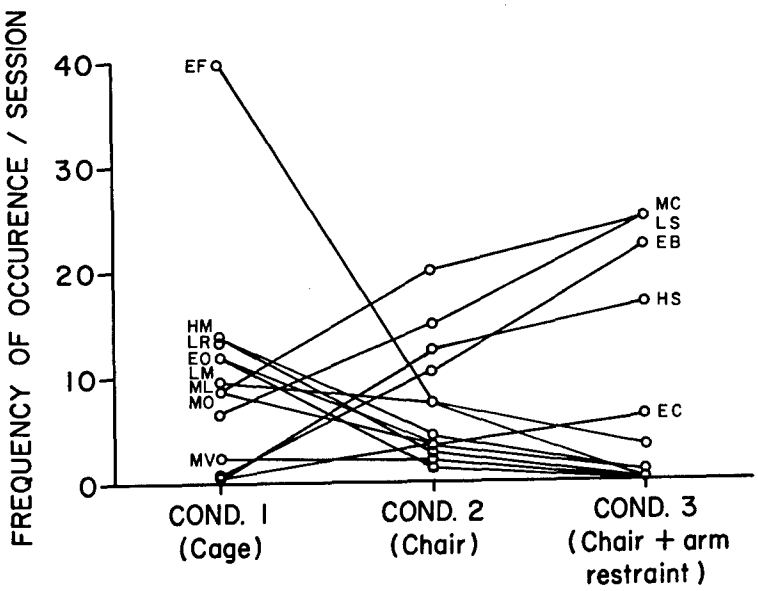

Figure 2. Frequency of occurrence of different behavior under varying conditions of restraint. Note that every behavior observed sequentially changed, incrementally or decrementally, with changing conditions of restraint. (See Table 1 for behavioral category legends).

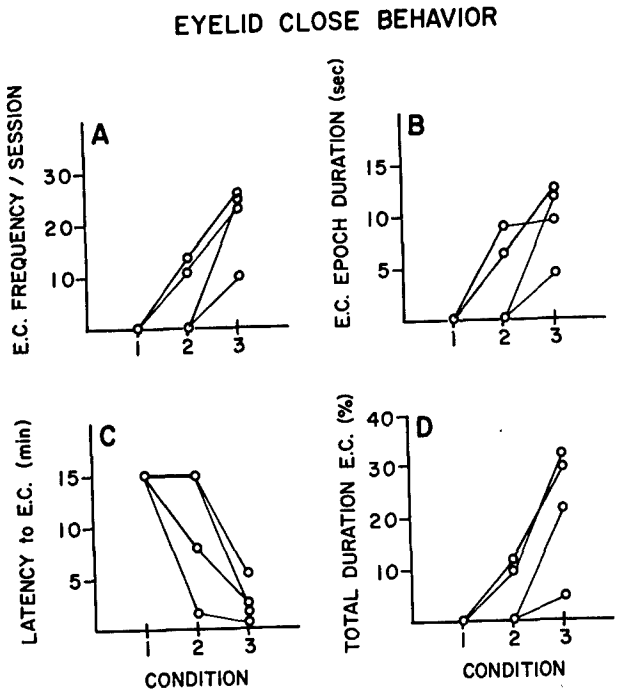

Figure 3. Eyelid closure (EC) behavior during 3 conditions of restraint. Each small graph (A-D) depicts the results of each of the four animals studied. Eyelid closure parameters displayed: A. Frequency per session. B. Average duration of each EC epoch. D. Latency to onset of EC from time of observation start. D. Cumulative total duration of EC as % of total duration of observation session.

EEG STUDY

Baseline EEG recordings showed a broad range of EEG activity from approximately 8 to 20 Hz with power spectral analysis. Similar spectra were seen from all central sulcal electrode pairs, between 2 and 30mm off center. During immobilization there was a striking enhancement of 12-15 Hz activity (Figure 4) correlated with a reduction of tone in all limbs, a reduction of spontaneous behavior, and an increased incidence of eyes closed behavior alternating with periods of blank staring. Spectral data from the three monkeys were analyzed in terms of absolute mean spectral power in each of three frequency bands: 8-11 Hz; 12-15 Hz; and 18-23 Hz. Overall mean values for each condition in the test sequence were determined, as shown in Figure 5. Although statistical analysis was deemed inappropriate due to the small number of animals, the resulting plots suggested that overall power was greatest in the 18-23 Hz range and comparable in the two other bands. With alerting, this power increased while 8-11 Hz decreased markedly and 12-15 Hz decreased to a lesser degree. Immobilization reversed this pattern, producing a sharp drop in 18-23 and increases in both 8-11 and 12-15 Hz activity. Alerting the immobilized animal again increased 18-23 and decreased 8-11, but did not alter 12-15 Hz activity. A return to baseline condition (i.e., removal of arm restraint) brought power spectral values close to their initial levels. Thus 12-15 Hz activity was related uniquely to immobilization independent of whether quieting or alerting factors were present. In general, the greatest degree of enhancement of 12-15 Hz activity with immobilization occurred at electrodes 12-22mm lateral to midline.

Quantitative analyses of spectral estimates are shown in Table 3 for the 3 animals in all conditions occurring with immobilization. Most commonly, the greatest magnitude of SMR activity occurring in the awake condition appeared during immobilization or during immobilization plus alerting stimuli. Specifically, 17 central sulci sites were analyzed; at 11 sites, SMR activity was highest during immobilization; and at 3 additional sites SMR activity was at a zenith during immobilization plus alerting stimuli.

DISCUSSION

A decrease in those behavior patterns characteristic of free-ranging animals and an increase in atypical inactivity was observed during progressive immobilization of the rhesus monkey. Therefore, we refer to this induced behavioral change as an immobilization response (IR). The IR, as observed and defined here, is similar to other behavioral phenomena described variously as animal magnetism, animal hypnosis, entrancement, akinesis, parosysmal inhibition, death-feigning, panic

reaction, still reaction, immobility reflex, catalepsy, tonic immobility, etc. (Chertok, 1968). Although historically many specialized techniques for inducing such phenomena have been documented, some degree of physical restraint seems to be present in all cases (Gillman et al., 1950).

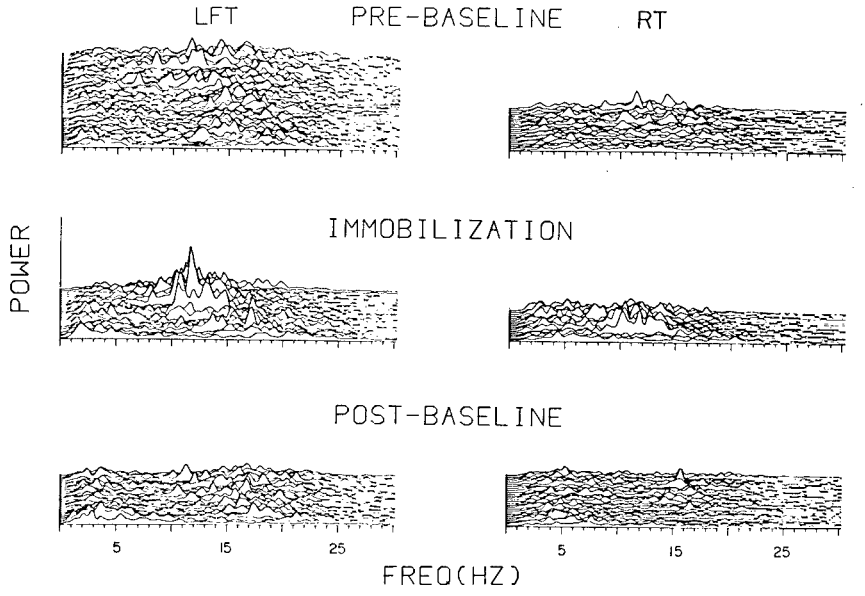

Figure 4. Power spectral analysis of EEG activity recorded from a pair of electrodes just anterior and posterior to central sulcus, 12mm off midline. Traces represent spectral distributions for successive 17.5 sec epochs of EEG activity plotted isometrically. Each plot, therefore, shows continuous data over 8-12 min quiet periods (no movement) in each condition. See text for details. The prominent right-left asymmetry during immobilization occurred commonly in this study.

TABLE 3

Quantitative analysis of absolute spectral power in each of three frequency bands (8-11 Hz, 12-15 Hz and 18-23 Hz). This table depicts data from all 3 animals (1, 2 and 3) under all experimental conditions (A-baseline, B-alert, C-immobilization, D-immobilization plus alert, E-baseline). Because of the magnitude of the quantitative data, values are shown only from left hemispheric sites 2mm, 12mm and 22mm off midline (L-2, L-12 and L-22) along the central sulcus. In all, a total of 17 sites were studied, 9 of which are summarized in this table.

	8-11 Hz					12-15 Hz					18-23 Hz				
Animal/ Site	A	B	C	D	E	A	B	C	D	E	A	B	C	D	E
1/L-2	9.04	7.96	12.62	7.98	7.07	11.61	8.91	14.91	10.09	7.99	29.39	34.39	23.62	33.68	36.95
2/L-2	12.32	7.71	14.45	14.20	12.36	9.26	7.59	10.02	14.88	9.61	16.07	18.38	18.46	23.75	18.79
3/L-2	16.56	14.13	19.55	20.43	15.64	16.81	16.49	15.54	19.67	15.98	16.35	20.33	13.91	13.83	18.47
$\bar{X}$	15.97	9.93	15.54	14.20	11.69	12.56	11.0	13.49	14.88	11.19	20.60	24.37	18.66	23.75	24.74
1/L-12	7.70	8.86	10.12	8.77	7.76	11.67	9.61	15.19	11.32	8.78	28.58	29.03	24.00	27.75	29.23
2/L-12	12.34	8.78	12.87	14.03	11.67	9.80	7.60	10.86	15.53	8.95	16.76	19.32	21.08	20.78	19.41
3/L-12	16.53	14.17	19.61	19.28	16.17	16.85	15.90	15.60	19.74	15.90	16.33	21.43	14.00	13.82	18.40
$\bar{X}$	12.19	10.60	14.20	14.03	11.87	12.80	11.04	13.88	15.53	11.21	20.56	23.26	19.69	20.78	22.35
1/L-22	5.18	5.13	8.80	4.17	4.52	16.13	14.32	19.05	12.01	9.84	38.03	38.54	31.11	40.95	40.90
2/L-22	18.44	18.20	17.42	8.32	17.87	11.50	11.85	11.39	13.88	12.52	9.63	11.64	9.39	29.00	10.68
3/L-22	12.68	11.33	13.55	12.46	11.0	14.40	13.73	15.24	15.15	12.62	17.87	19.60	13.67	17.05	18.91
$\bar{X}$	12.1	11.55	13.26	8.32	11.13	14.01	13.30	15.23	13.58	11.66	21.84	23.26	18.06	29.00	23.50

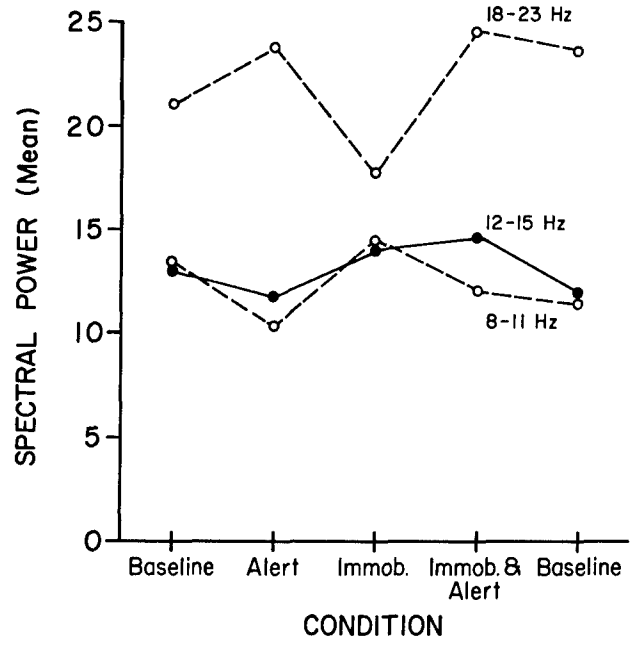

Figure 5. Mean spectral power in each of three frequency bands (8-11 Hz, 12-15 Hz and 18-23 Hz) under conditions described along abscissa. Note that only in the 12-15 Hz band does the power remain relatively constant whether the animal is immobilized in a quiet environment or is immobilized amidst alerting stimuli. Data points represent mean of all central sulci recording sites from all animals.

The relationship between the IR and SMR activity was predicted because of the behavioral similarities between the primate IR and subjects (cat or man) operantly conditioned to produce enhanced 12-15 Hz activity. In both situations there appears to be a correlation between 12-15 Hz EEG activity and a relaxed, relatively immobile positioning. In fact, current SMR research began with the observation that cats given food for becoming immobile developed 12-15 Hz activity inextricably linked to the behavioral immobility (Sterman and Wyrwicka, 1967); further, if just the 12-15 Hz activity was operantly conditioned, the animals always assumed an immobile posture as criteria EEG activity appeared (Wyrwicka and Sterman, 1968). SMR activity was enhanced also in relation to reduced somatosensory input resulting from lemniscal lesions (Elliot and Sterman, 1975). The anatomical and physiological basis of the SMR, as well as the behavioral importance of SMR, is currently under investigation.

The particular relationship between immobility and 12-15 Hz EEG activity was enhanced by alerting the immobilized animal. First, 18-23 Hz activity may have been interpreted as being inversely related to immobilization since overall power was greatest in this range at rest, and since such activity sharply declined with immobilization. Second, 8-11 Hz overall power was comparable to that in the 12-15 Hz range at rest, and increased during immobilization suggesting a direct correlation between immobility and 8-11 Hz activity. However, the critical manipulation involved alerting the immobilized animal: 12-15 Hz activity remained unaltered; 8-11 Hz activity sharply declined; and 18-23 activity increased. Thus, 8-11 Hz activity was inversely related to the level of alertness (i.e., directly related to drowsiness), 18-23 Hz activity was directly related to the degree of arousal, but 12-15 Hz activity emerged as uniquely and directly related to immobility. This relationship was independent of the level of arousal in the awake animal.

We were impressed by the fact that the immobilization response continued throughout the 15 minute observation interval, but both behaviorally and electroencephalographically the IR appeared to consist of interrupted short interval components. Periods of relaxed immobility would alternate with brief intervals of restless struggling, but there were consistent correlative EEG changes in that enhanced SMR activity appeared only during periods of relaxed immobility. In general, most uninterrupted intervals of the IR were between one-half and four minutes in duration.

The immobilization response and associated EEG changes appear to characterize a specific state of central nervous system organization. Moreover, this altered state was found to be inhibitory to seizures resulting from exposure to MMH in cats. The neurophysiological and therapeutic implications of these relationships are clearly worthy of further investigation.

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PART 2. OPERANT CONDITIONING OF 12-15 HZ SENSORIMOTOR CORTEX EEG ACTIVITY IN THE RHESUS MONKEY

INTRODUCTION

Previous work in our program has shown that operant conditioning of rhythmic 12-15 Hz sensorimotor cortex EEG activity in the cat (the sensorimotor rhythm or SMR) resulted in decreased susceptibility to seizures produced by exposure to convulsive doses of monomethylhydrazine (MMH) (Sterman et al, 1969; Sterman, 1976). Other studies have indicated that imposed immobilization (bagging) of the cat both induced SMR activity and raised seizure thresholds in response to MMH exposure (Bowersox et al., in press). Since one of our primary objectives in this program was to evaluate the neurophysiological basis for this protection, it was deemed desirable to establish a more appropriate experimental model for its study. The rhesus monkey (Macaca mulatta) was chosen in this regard because of the obvious advantage of the primate, and because other studies with this animal had demonstrated the presence of SMR activity, specifically during imposed restraint (Part 1, this report).

Our initial task in this effort was to determine whether or not the rhesus could be operantly conditioned to produce SMR activity, as had been demonstrated with the cat. Subsequent studies would then explore the effects of this training upon seizure mechanisms and associated susceptibility to MMH. The present report documents the success achieved in accomplishing this initial task.

METHODS

Four female rhesus monkeys weighing between 4 and 6 kg were thoroughly adapted to primate restraining chairs over a 2 month interval. Then, using ketamine anesthesia and sterile surgical techniques, a bilateral frontal-parietal craniotomy was done. The dura was opened, and specific sulcal anatomy was noted and translated to the bone flap. The dura was then closed, the bone flap was wired into place, and a series of 3mm holes were drilled through the calvarium in relation to the central sulcus, i.e., 2mm anterior and 2mm posterior to the central sulcus located 2, 12, 22, and 32mm from midline, bilaterally. Silver-ball electrodes were then positioned through the calvarial openings so that they rested directly upon the dura. Insulated leads were collected into a subminiature Winchester connector that was secured to the skull with fixation screws and methyl methacrylate. The scalp was partially closed and the animals returned to their primate chairs. After a one-month recovery, the animals were started on a training schedule.

Initially the animals were adapted to a sound-attenuating isolation chamber. The entire chair was transferred into the chamber, and a food cup was clamped to the waist plate. A motorized food hopper outside the chamber was connected to the cup via hollow tubing, and with each step advance of the hopper a single 50 mg food pellet was delivered to the food cup. The animals rapidly learned to remove pellets from the cup and feed themselves through an open porthole in the neck plate. The feeding

schedule was adjusted so that each animal would promptly empty the cup and eat at least 100 pellets when brought into the chamber on a Monday-Wednesday-Friday pattern.

Training was begun after preliminary studies indicated that the most easily detected SMR activity appeared at mid-lateral electrodes (i.e., leads 12 or 22mm off midline). Each animal was then trained only to a single mid-lateral electrode site over the left hemisphere. EEG activity from that electrode site was led to a logic circuit containing sharply tuned frequency filters set at 8-11 Hz and 12-15 Hz. The output of this logic circuit was a signal sufficient to trigger the release of one pellet from the feeder. Initial recordings were obtained from each animal for the purpose of adjusting EEG amplifications to comparable displays and for the purpose of adjusting the 8-11 Hz and 12-15 Hz amplitude "window" to comparable levels. Thereafter, all gains used for each animal were left unchanged for the several months of training. The criterion for a pellet reward was the presence of a 0.5 second burst of 12-15 Hz, the absence of 8-11 Hz, and the absence of short duration high voltage transients (movement artifacts). This criterion remained unchanged except that as reinforcements increased in frequency approaching one minute, the required duration of the 12-15 Hz burst increased by 0.5 second intervals from 0.5 to 1.0, and finally to 1.5 seconds.

Training sessions were conducted on a fixed schedule three times per week for 12 weeks. Each session was one hour long for three animals, and 40 minutes long for the fourth animal.

During two of the three sessions per week the following data were continuously recorded on a polygraph and on magnetic tape: Unfiltered EEG activity from the "training" electrode pair; the outputs from the 8-11 and the 12-15 Hz filters; and a marker indicating each reinforcement. During one training session each week, polygraphic and magnetic tape recordings were obtained in all animals from multiple electrode sites along sensorimotor cortex in addition to activity recorded from the "training" electrode. These data are now being prepared for quantitative analysis.

PRELIMINARY RESULTS

Operant conditioning was successfully accomplished in each animal in that increased 12-15 Hz activity appeared from sensorimotor cortex during training sessions. Initially animals received between 15 and 30 reinforcements per session, but by the third week of training all animals were receiving more than 40 reinforcements per session. After different lengths of training (one at fifth week, two at seventh week, one at tenth week) each animal was able to maintain a satisfactory rate of reinforcement even when the requisite SMR burst duration was increased from 0.5 to 1.0 seconds. Further, two animals eventually produced sufficient SMR activity to maintain good reinforcement rates (approximately 50 per session) when 1.5 second bursts of 12-15 Hz were required.

The behavior of the animals changed during training. All animals appeared to be restfully calm and awake while producing criterion SMR. Often their hands were folded limply, and at times the animals fixed gaze steadily at one point. Two animals were frequently quite restless between periods of SMR production; over the period of 12 weeks there was a dramatic reduction in restless activity during training sessions.

The polygraphically recorded EEG changed steadily during training. Initially it was difficult to detect overt EEG changes at the instant that the animal was reinforced. There was a progressive augmentation of 12-15 Hz activity, first appearing as a "ripple" in the EEG, and eventually dominating the EEG by long duration high voltage trains (Figure 1). In some instances the conventially recorded EEG began to resemble the activity recorded as the restricted output from the 12-15 Hz filter.

DISCUSSION

SMR activity, defined specifically as a 12-15 Hz rhythm recorded from sensorimotor cortex, can be operantly conditioned in the rhesus monkey. Learning occurs rapidly and, as the animals achieve a higher reinforcement rate, striking changes appear in the EEG that are obvious to simple visual inspection of the record.

Patients with epilepsy who are provided with training to produce enhanced SMR activity show a corresponding reduction in the incidence of seizures (Sterman et al., 1974; Wyler et al., 1976; Lubar and Bahler, 1976). However, even after extensive training, visual detection of SMR activity in a conventionally recorded EEG is difficult. Epileptic patients may not produce prominent SMR activity because of their underlying disease, medications, species differences (vs. monkeys); attenuation effects from scalp recordings in contrast to monkey epidural recordings, etc. (Sterman, 1977). Thus, this primate model uniquely permits a systematic study of SMR activity since such activity is readily conditioned and is easily detected.

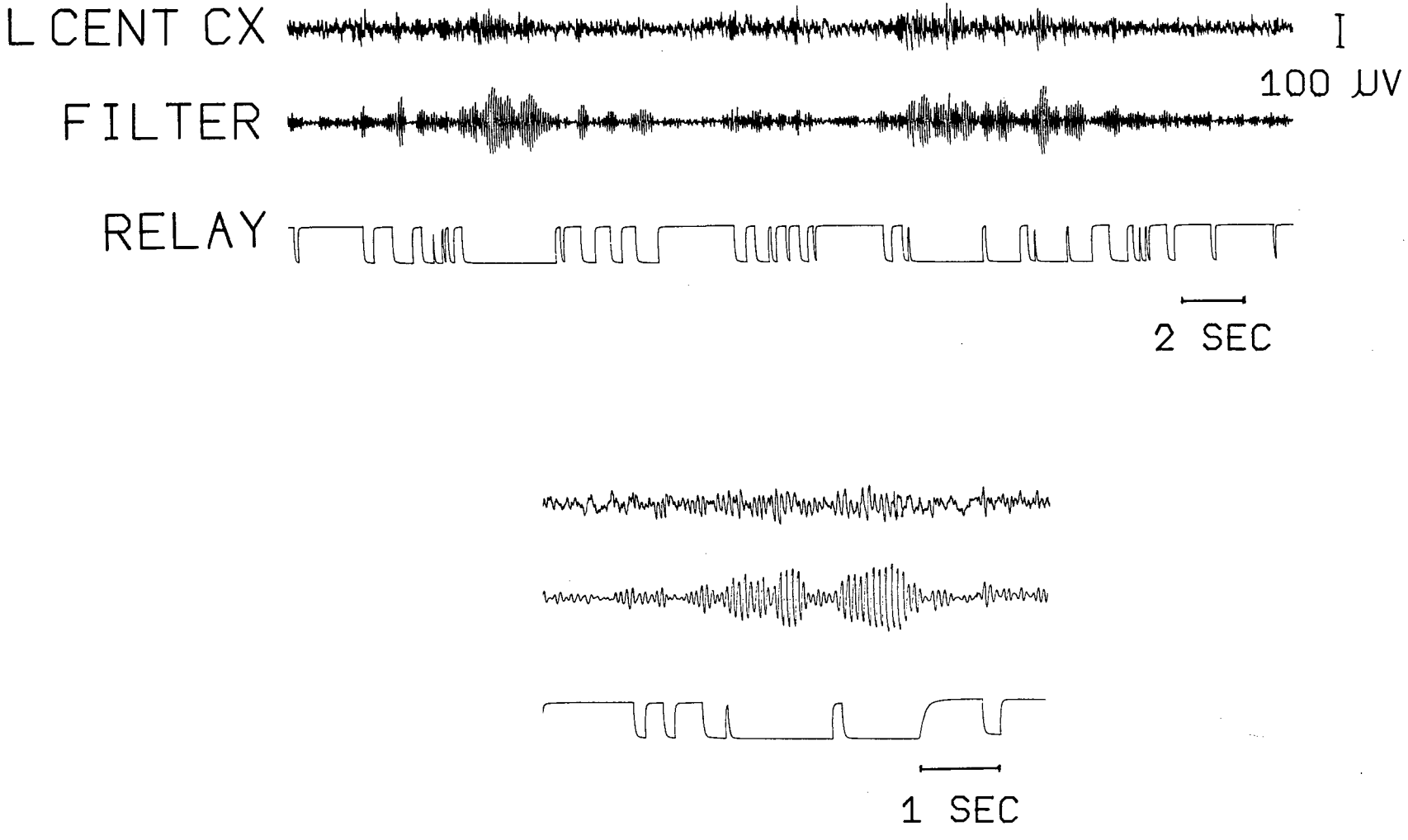

Figure 1. Sample tracing from left sensorimotor cortex in rhesus monkey trained to produce 12-15 Hz activity for food reward. Discharge of tuned 12-15 Hz filter is shown also, together with detection relay. Insert at bottom shows similar trained EEG response at faster paper speed.

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